

In the Claims

1. (Withdrawn) An *in vitro* method for detecting the presence of a demyelinating disease in an individual, for determining the stage or severity of said disease in the individual, or for monitoring the effect of the therapy administered to an individual presenting said disease, comprising:
 - a) detecting and/or quantifying the DUSP6 protein, the *dusp6* gene mRNA, or the corresponding cDNA in a sample of said individual, and
 - b) comparing the DUSP6 protein amount, the *dusp6* gene mRNA amount, or the corresponding cDNA amount detected in a sample of an individual, with the DUSP6 protein amount, with the *dusp6* gene mRNA amount, or with the corresponding cDNA amount detected, respectively, in samples from control individuals or with normal reference values.
2. (Withdrawn) A method according to claim 1, wherein the demyelinating is selected from the group consisting of multiple sclerosis, Devic's syndrome, Baló disease, Marchiafava-Bignami disease, central pontine myelinolysis, acute disseminated encephalomyelitis, and acute necrotizing hemorrhagic encephalomyelitis.
3. (Withdrawn) A method according to claim 1, wherein said sample is selected from the group consisting of serum, urine, saliva, feces, and cerebrospinal fluid.
4. (Withdrawn) A method according to claim 3, wherein said sample is obtained by surgical resection.
5. (Withdrawn) A method according to claim 1, wherein said sample is obtained from an individual who has not previously been diagnosed with a demyelinating disease.
6. (Withdrawn) A method according to claim 1, wherein said sample to analyze is obtained from an individual who has previously been diagnosed with a demyelinating disease.
7. (Withdrawn) A method according to claim 1, wherein said sample to analyze is obtained from an individual undergoing treatment, or who has been previously treated against a demyelinating disease.
8. (Withdrawn) A method according to claim 1, further comprising carrying out an extraction of the sample to obtain a protein extract or to obtain an extract consisting of total RNA.

9. (Withdrawn) A method according to claim 8, characterized in that the detecting of the DUSP6 protein comprises contacting the protein extract of the sample with a composition of one or more specific antibodies against one or more epitopes of the DUSP6 protein, and quantifying the complexes formed by the antibodies and DUSP6 protein.

10. (Withdrawn) A method according to claim 9, characterized in that said antibodies comprise a species selected from the group consisting of monoclonal antibodies, polyclonal antibodies, intact or fragments thereof, recombinant fragments thereof, "combibodies," Fab antibody fragments, and scFv antibody fragments.

11. (Withdrawn) A method according to claim 10, characterized in that the complexes formed by the antibodies and the DUSP6 protein are quantified using a technique selected from the group consisting of Western-blot, ELISA (Enzyme-Linked Immunosorbent Assay), RIA (Radioimmunoassay), Competitive EIA (Competitive Enzyme Immunoassay), DAS-ELISA (Double Antibody Sandwich-ELISA), immunocytochemical techniques, immunohistochemical techniques, techniques based on the use of protein biochips, techniques based on the use of microarrays including specific antibodies, assays based on precipitation with colloidal gold, affinity chromatography techniques, ligand binding assays and lectin binding assays.

12. (Withdrawn) A method according to claim 8, characterized in that the detecting of mRNA comprises a first amplification step of the mRNA included in the total RNA extract, and a second quantification step of the amplification product of the mRNA of the *dusp6* gene.

13. (Withdrawn) A method according to claim 12, characterized in that the amplification is carried out by means of RT-PCR using oligonucleotide primers wherein the sequences of the primers used to amplify the *dusp6* gene sequence are selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, and any other primer pair amplifying *dusp6*.

14. (Withdrawn) A method according to claim 8, characterized in that the detecting of mRNA is carried out by specific probes of mRNA or the corresponding cDNA probes of the *dusp6* gene.

15. (Withdrawn) A method according to claim 8, characterized in that mRNA detection is carried out by means of real time quantitative RT- PCR (Q-PCR).

16. (Cancelled)

17. (Withdrawn) An *in vitro* method for identifying and evaluating the efficacy of an agent for therapy of demyelinating diseases, said method comprising:

- a) treating a primary culture of rat optic nerve oligodendrocytes with stimuli relevant to demyelinating diseases to produce a culture of stimulated oligodendrocytes,
- b) detecting and quantifying changes in *dusp6* gene or DUSP6 protein expression in cells of the culture of stimulated oligodendrocytes in response to said stimuli,
- c) contacting the culture of stimulated oligodendrocytes with the agent under conditions and for time suitable for permitting interaction between the stimulated oligodendrocytes and the agent to form interacting stimulated oligodendrocytes,
- d) detecting and quantifying the *dusp6* gene or DUSP6 protein expression levels in the culture of interacting stimulated oligodendrocytes, and
- e) comparing the expression levels obtained in step d) with the corresponding levels in the culture of stimulated oligodendrocytes not treated with the agent.

18. (Cancelled)

19. (Currently Amended) A method for the reducing the activity of the DUSP6 protein, the method comprising administering an effective amount of an agent treatment of the neurodegenerative phase of demyelinating diseases, which comprises the administration of an agent that inhibits DUSP6 protein expression and/or activity to reduce excitotoxic death of oligodendrocytes in an individual having multiple sclerosis, or that inhibits the lethal effects of induction of DUSP6 protein expression.

20. (Currently Amended) The method according to claim 19 wherein said agent comprises is selected from the group consisting of:

- a) an antibody, or combination of antibodies, specific against one or more epitopes present in the DUSP6 protein, wherein said antibody comprises a human monoclonal antibody, a humanized monoclonal antibody a fragment of the antibody, a single chain antibody or an anti idiotypic antibody,
- b) cytotoxic agents selected from the group consisting of toxins, molecules with radioactive atoms, and chemotherapeutic agents, and
- e) DUSP6 protein antagonist compounds inhibiting one or more of the DUSP6 protein functions.

21. (Cancelled)

22. (Withdrawn) A dusp6 specific antisense oligonucleotide selected from the group consisting of SEQ ID NO:3 and SEQ ID NO:4.

23. (Withdrawn) A kit for an *in vitro* method of detecting the presence of a demyelinating disease in an individual, said kit comprising an antibody that specifically recognizes the DUSP6 protein and a carrier in suitable packing.

24. (Withdrawn) A kit for an *in vitro* method of detecting the presence of a demyelinating disease in an individual, said kit comprising a primer pair designed to specifically amplify a nucleic acid having a sequence that is specific to the dusp6 gene.

25. (Withdrawn) A kit according to claim 24, wherein the sequence of the primer pair is selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2.

26. (Withdrawn) A kit according to claim 23 that is employed to detect the presence of demyelinating diseases in an individual, to determine the stage or severity of said conditions in an individual or to monitor the effect of the therapy administered to the individual with said conditions.

27. (Withdrawn) A method according to claim 8, characterized in that the detecting of corresponding cDNA dusp6 gene comprises a first amplification step of the corresponding cDNA synthesized by reverse transcription of the mRNA, and a second quantification step of the amplification product of the cDNA of the dusp6 gene.